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| APPLICATION NO | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO |
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| 09/670,756 | 09/27/2000 | Kenneth Rhodes | MNI-070CP4 | 6507 |

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LAHIVE & COCKFIELD
28 STATE STREET
BOSTON, MA 02109

| EXAMINER |
|---|
| MURPHY, JOSEPH F |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1646 | |

DATE MAILED: 05/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/670,756 | RHODES ET AL. | |
| | Examiner | Art Unit | |
| | Joseph F Murphy | 1646 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)[X] Responsive to communication(s) filed on *14 March 2003* .

2a)[ ] This action is **FINAL**. 2b)[X] This action is non-final.

3)[ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)[X] Claim(s) *8,10,57,58 and 61-67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)[X] Claim(s) *63-64* is/are allowed.

6)[X] Claim(s) *8, 10, 57-58, 61-62, 66-67* is/are rejected.

7)[ ] Claim(s) _____ is/are objected to.

8)[ ] Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)[ ] The specification is objected to by the Examiner.

10)[ ] The drawing(s) filed on _____ is/are: a)[ ] accepted or b)[ ] objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)[ ] The proposed drawing correction filed on _____ is: a)[ ] approved b)[ ] disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)[ ] The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)[ ] Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)[ ] All b)[ ] Some * c)[ ] None of:

1.[ ] Certified copies of the priority documents have been received.

2.[ ] Certified copies of the priority documents have been received in Application No. _____ .

3.[ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)[ ] Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) [ ] The translation of the foreign language provisional application has been received.

15)[ ] Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) [ ] Notice of References Cited (PTO-892)
2) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) [ ] Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) [ ] Interview Summary (PTO-413) Paper No(s).
5) [ ] Notice of Informal Patent Application (PTO-152)
6) [ ] Other:

## DETAILED ACTION

### *Formal Matters*

Claims 55, 56, 59 and 60 were cancelled, and claims 8, 10, 57, 58, 61, 62, 63, 64, 65 were amended, and new claims 66-67 were added in Paper No. 3/14/2003. Claims 8, 10, 57-58, 61-67 are pending and under consideration.

### *Information Disclosure Statement*

References D8 to E12 on the IDS filed 1/20/2001 have been lined through because it is not in the correct format. The citation should include the author and publication date. However, without relevant sequence alignment data to the SEQ IDs of the present claims, relevance cannot be ascertained, regardless.

### *Response to Amendment and Arguments*

The rejection of claims 55, 59 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention due to the limitation of "allelic variant" recited in the claim Has been obviated by Applicant's amendment and is thus withdrawn.

The rejection of claims 55, 59 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

obviated by Applicant's amendment and is thus withdrawn.

The rejection of claims 56, 60 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6117989 (Bandman et al.) has been obviated by Applicant's amendment, and is thus withdrawn.

***Claim Rejections - 35 USC § 112 first paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8, 10 and 57-58, 61-62, stand rejected, and new claims 66-67 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an amino acid of SEQ ID NO: 20, does not reasonably provide enablement for an amino acid sequence which is 90%, 95% identical to SEQ ID NO: 20, or an amino acid sequence which comprises at least 15 contiguous amino acids of SEQ ID NO: 20 or a polypeptide comprising 15 amino acids of SEQ ID NO: 20, comprising a calcium binding domain, for reasons of record set forth in Paper No. 14, 12/13/2002. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims encompass an amino acid sequence which is 90%, 95% identical to SEQ ID NO: 20, or an amino acid sequence which comprises at least 15 contiguous amino acids of SEQ ID NO: 20 or a polypeptide comprising 15 amino acids of SEQ ID NO: 20, comprising a calcium binding domain. The specification discloses that the polypeptide of SEQ ID NO: 20 (PCID 9qm) colocalized with Kv4.2 and Kv4.3 channels, and claims that the encompassed polypeptides can "interact" with a potassium channel. The art teaches that even single amino acid changes or

differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. For example, Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph). Since the claims encompass variant nucleic acids and given the art recognized unpredictability of the effect of mutations on protein function, it would require undue experimentation to make and use the claimed invention. The Voet reference demonstrates that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. Working examples are provided for SEQ ID NO: 20. Given the breadth of claims 8, 10, 57-58, 61-62, 66-67 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Applicant argues that the claims include a functional limitation wherein the polypeptide is capable of interacting with a potassium channel. However, claims 8 and 10 do not include a functional limitation for the claimed polypeptides. Additionally, newly presented claims 66 and 67 also do not contain a functional limitation for the claimed polypeptides, they are only drawn to polypeptides that comprise a calcium binding domain. Since detailed information regarding

the structural and functional requirements of the peptides are lacking, it is unpredictable as to which encoding variations, if any, meet the limitations of the claims. Furthermore, since the claims encompass an amino acid sequence which is 90%, 95% identical to SEQ ID NO: 20, or an amino acid sequence which comprises at least 15 contiguous amino acids of SEQ ID NO: 20 or a polypeptide comprising 15 amino acids of SEQ ID NO: 20, comprising a calcium binding domain, while the claims do not recite a functional limitation for the encompassed amino acid sequences, there is not sufficient direction as to how to use the encompassed polypeptides which do not interact with a potassium channel. Since no functional language is associated with claims 8, 10 and 66-67, one of ordinary skill in the art would not know how to use these defined sequences except in further characterization of the sequences themselves.

Applicant argues that with regards to claims 57-58 and 61-62, the claims are similar to Example 14 of the Revised Interim Written Description Guidelines, wherein protein variants that are 95% identical to a sequence and that catalyze a reaction meet the written description requirement. In the instant case, claims 57-58 and 61-62 are drawn to polypeptides that are capable of interacting with a potassium channel. However, this is not a specific functional limitation for the claimed polypeptides since the term "interacting" is indefinite (see *infra*). It is not clear whether the polypeptides encompassed by the claim must actually bind and modulate the potassium channel, or are associated with a potassium channel in some other way, or simply "interact" with the potassium channel simply by being in the same cell. Changing the functional limitation to make it clear that the encompassed polypeptides can bind and modulate the potassium channel activity would obviate this rejection. Additionally, Example 14 is from

the Written Description Guidelines, and is exemplary of a claim that meets the Written Description requirement, while the instant rejection is for lack of enablement.

Claims 8, 10 and 57-58, 61-62, stand rejected, and new claims 66-67 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for reasons of record set forth in Paper No. 14, 12/13/2002. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

These are genus claims. The claims are drawn to amino acid sequences which are 90%, 95% identical to SEQ ID NO: 20, or an amino acid sequence which comprises at least 15 contiguous amino acids of SEQ ID NO: 20 or a polypeptide comprising 15 amino acids of SEQ ID NO: 20, comprising a calcium binding domain. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The specification and claim do not place any limits on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to the encoded SEQ ID NO: 20. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and

claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the polypeptide of SEQ ID NO: 20 is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Applicant argues that with regards to claims 57-58 and 61-62, the claims are similar to Example 14 of the Revised Interim Written Description Guidelines, wherein protein variants that are 95% identical to a sequence and that catalyze a reaction meet the written description requirement. In the instant case, claims 57-58 and 61-62 are drawn to polypeptides that are capable of interacting with a potassium channel. However, as set forth above, claims 57-58 and 61-62 are drawn to polypeptides that are capable of interacting with a potassium channel. However, this is not a specific functional limitation for the claimed polypeptides since the term "interacting" is indefinite (see *infra*). It is not clear whether the polypeptides encompassed by [illegible] potassium channel in some other way, or simply "interacts" with the potassium channel simply by being in the same cell. Changing the functional limitation to make it clear that the

encompassed polypeptides can bind and modulate the potassium channel activity would obviate this rejection.

Additionally, Applicant argues that regarding claim 8, 10 and 66-67 because it is similar to Example 15 of the Written Description Guidelines. In Example 15 of the Written Description Guidelines a claim drawn to an antisense oligonucleotide complementary to an mRNA having a certain sequence, and wherein the oligo inhibits the production of human growth hormone, is adequately describe. Applicant argues that since one of skill in the art would be able to envisage members of the genus embraced by the claims the claims adequately describe the invention. However, in contrast to Example 15, claims 8 and 10 do not include a functional limitation for the claimed polypeptides. Additionally, newly presented claims 66 and 67 also do not contain a functional limitation for the claimed polypeptides, they are only drawn to polypeptides that comprise a calcium binding domain. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide

claimed genus of polynucleotides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure

to function. Structural features that could distinguish the compounds in the genus from other seven transmembrane region compounds are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides encompassed: there is no guidance in the art as to what the defining characteristics of the peptides might be. As is set forth in Example 15 of the Written Description Guidelines, the antisense oligo is adequately described for three reasons: i) the sequence allows one of skill in the art to envisage members of the genus; ii) the functional characteristics of the claimed invention are set forth, along with art recognized methods for screening; iii) the general level of knowledge and skill in the art. In the instant case, no functional characteristics of the claimed invention are set forth for claims 8, 10 and 66-67. Thus, no identifying characteristics or properties of the instant polynucleotides are provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed.

Claim 65 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention.

The deposit of the biological material is considered necessary for the enablement of the current invention (see MPEP Chapter 2400 and 37 C.F.R. §§ 1.801-1.809). Elements required

for practicing a claimed invention must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. Applicants have provided the deposit number for plasmid 98991 and 98993, but the specification is not fully compliant with all of the provisions for maintenance and availability of the deposited material. If a deposit is made under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure (e.g. see 961 OG 21, 1977), and Applicants, their assignee or their agent needs to provide a declaration containing the following: i) a statement all restrictions on the availability to the public of the deposited material so deposited will be irrevocably removed upon the granting of a patent. ii) A statement that the material has been deposited under conditions that assure that access to the material will be available during the pendancy of the patent application to one determined by the Commissioner to be entitled thereto under 37 C.F.R. 1.14 and 35 U.S.C. § 122. iii) A statement that the deposited material will be maintained with all of the care necessary to keep it viable and uncontaminated for a period of at least five years after the most recent request for the furnishing of a sample of the deposited microorganism, and in any case, for a period of at least thirty years after the date of deposit or for the enforceable life of the patent, whichever period is longer. iv) A statement by declarant that all statements are true and that all statements made on information and belief are believed to be true; and further that these statements were made on information and belief with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code and that such willful false

statements may jeopardize the validity of the instant patent application or any patent issuing thereon.

***Claim Rejections - 35 USC § 112 second paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 57-58, 61-62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 57-58, 61-62 are vague and indefinite in the recitation of the term "interaction". It is not clear whether this term limits the polypeptide to one which binds the potassium channel, or whether the polypeptide may modulate some other function that the potassium channel has ina process other than binding. The metes and bounds of the claims cannot be determined.

***Conclusion***

Claims 63-64 are allowable.

Claims [illegible] are rejected.

***Advisory Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
May 20, 2003

GARY KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600